WELCOME

Dear Colleague:

The National Institutes of Health is pleased to invite you to the second annual symposium on the Functional Genomics of Critical Illness and Injury, to be held November 17th and 18th at the Natcher Conference Center, National Institutes of Health, Bethesda, Maryland.

The first symposium on this important and timely topic, which took place in April 2002, was aimed at defining this emerging field and providing a forum for building a research agenda. The upcoming event will provide further opportunities for communication among experts in the various disciplines of critical care medicine and the field of functional genomics. It will showcase the latest research findings, facilitate the exchange of information on state-of-the-art methodologies, and highlight the challenges we face now and in the future. Knowledge emerging from functional genomic databases and presentation of primary clinical and experimental data on critical illness are the centerpieces of this year's symposium. The agenda will also include an expanded proteomics section as well as pharmacogenomics and modeling. Oral abstracts and poster sessions that allow one-on-one discussions between presenters and participants will be integrated into the program along with featured speakers. This more intimate setting will allow participants to gain deeper insights into topics and issues most relevant to their own work.

We will be accepting registrations and abstract submissions in Summer 2003. All registrants from the first symposium will be contacted by e-mail to guide them to the updated registration site on the Web.

This symposium is a unique opportunity for exchange of ideas among the diverse fields committed to applying lessons from functional genomics at the bedside of critically ill and injured patients. We look forward to welcoming you to Bethesda this November.

Sincerely,

The Organizing Committee

Anthony F. Suffredini, M.D. National Institutes of Health

Robert L. Danner, M.D. National Institutes of Health

J. Perren Cobb. M.D. Washington University School of Medicine

Peter Munson, Ph.D. National Institutes of Health

Scott Somers, Ph.D.

National Institutes of Health

GENERAL INFORMATION

Dates

November 17- 18, 2003

Location

National Institutes of Health Natcher Conference Center Bethesda, Maryland

Program At-A-Glance Speaker Presentations:

November 17, 2003 November 18, 2003

Poster Session:

November 17, 2003

Oral Abstracts:

November 17, 2003

November 18, 2003

Exhibits:

November 17, 2003

Conference Fee

The conference fee for this event is \$125.

There is no fee for federal employees, and in training.

Register

Registration closes November 11, 2003.

Call for Abstracts



INTRODUCTION

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At first glance, it is difficult to see how the urgent nature of critical care medicine relates to the highly technical, research-centered field of functional genomics. The typical portrait of intensive care comprises beeping monitors, tubes, multiple laboratory tests, IVs full of broad spectrum antibiotics, and, often, uncertainty about whether a patient will survive. By contrast, the popular notion of genetic technologies is DNA fingerprinting and the investigation of rare diseases caused by single gene mutations. Neither conception reflects the whole picture. The recent completion of the human genome project and parallel developments in high-throughput biology have made it possible to examine complex diseases in unprecedented detail. Knowledge of species-specific biological responses to injury and infection at the molecular level, gleaned through functional genomics, has the potential to launch critical care medicine into a new, more refined, era.

The example of multiple organ dysfunction syndrome (MODS) illustrates a specific potential application of functional genomics to critical care: Severe infection and traumatic injury are often complicated by multiple organ failures that cause substantial illness and death. Components of MODS include septic shock, acute respiratory distress syndrome, acute renal failure, hepatic injury, myocardial dysfunction, coagulopathic states, and encephalopathy, all of which may be viewed as host responses to a critical insult. Alone and cumulatively, each of these conditions increases the risk of death even after successful treatment of the underlying infection or injury. Yet, despite substantial effort, treatments directed at a single mediating gene or inflammatory pathway have done little to alter the outcomes of critically ill patients. With a functional genomic approach, however, these conditions could be viewed and interpreted at multiple levelsfrom the organ to the genome--more accurately reflecting the interactive, emergent properties of adaptive and maladaptive host responses.

As functional genomics begins to translate knowledge from the research laboratory to the bedside, intensivists will have a new set of tools to complement or even replace the old ones: high-throughput technologies such as microarrays, highly parallel single nucleotide polymorphism analysis, and proteomics. As always, their goal will be to develop a more global understanding of complex biologic processes and systems, integrating pathophysiology, cell biology, and prewired genetic programs.

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BACKGROUND TO THE CONFERENCE

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Critical care medicine is a multidisciplinary endeavor that crosses traditional departmental and specialty lines. Despite large health care expenditures for critical care services, no single institute at the NIH specifically focuses on the critically ill or injured patient. On the functional genomics side, the massive amount of data generated by its technologies calls out for further collaboration, not just among medical specialties but between the medical community and biostatisticians, mathematicians, computer scientists, and computational biologists. To focus attention on both the integrative demands of critical care medicine and the need for close communication with experts in functional genomic technologies, the NIH sponsored its first symposium on Functional Genomics of Critical Illness and Injury, which was held at the Clinical Center in April 2002. This gathering was sponsored jointly by the Clinical Center, NIGMS, NIAMS, NHLBI, NHGRI, and NIAID with the help of the NIH Foundation and support from four international medical societies. Health care providers, physiologists, molecular biologists, genomicists, and biostatisticians gathered for three days to discuss the impact of genomics and proteomics on the science and practice of critical care medicine.

Four hundred participants representing more than ten countries heard presentations spanning a range of biologic complexity, from genome to population. Thirty leaders in their respective fields spoke on topics such as the clinical epidemiology of critical illness and injury, biocomplexity, investigational therapies, genome-wide expression profiles in trauma and infection, functional aspects of genetic variability in the intensive care unit, genomic studies of host-pathogen interactions, applications for defense against bioterrorism, and the future of computational genomics.

Attendees uniformly hailed the conference as a watershed event. Three general themes emerged from comments and suggestions of the participants: First and most importantly, the symposium should be held annually. Second, increased collaboration should develop between those who generate the data (experimentalists) and those who analyze it (informaticists). Third, the experimental designs and analytic standards developed by centers with the greatest expertise should be shared widely to optimize the use of resources and data.

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FOCUS OF THE SECOND CONFERENCE

The second symposium will bring together once again multidisciplinary critical care specialists (e.g., intensivists from internal medicine, surgery, pediatrics, and anesthesiology), microbiologists, molecular biologists, experts in high-throughput technologies, and computational scientists to discuss the application of functional genomic approaches to critical illness and injury. This time it will focus on knowledge emerging from functional genomic databases relevant to critical care medicine and provide a forum for the presentation of primary data from patients and models of critical illness. The section on proteomics will reflect new developments in this field, especially in novel protein signatures and biomarkers of pathologic states. Pharmacogenomics as it applies to critically ill and injured patients is another major area included in this year's event. In addition to featured speakers, invited presentations and poster sessions will allow one-on-one discussions between presenters and participants.

The second symposium will also address policy issues raised by the special demands of functional genomics on resources and experimental design. Investigators who plan to use genomic approaches to study critical illness and injury face major challenges from private laboratories, academic departments, and public funding agencies. The symposium will address these uncertainties and disseminate consensus opinions through a published summary of the meeting.

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Call for Abstracts



Registration

Abstracts

Contacts

ORGANIZING COMMITTEE

Co-Chairs

Anthony F. Suffredini, M.D.

ORGANIZING COMMITTEE

Critical Care Medicine Department

Clinical Center

Bethesda, MD

J. Perren Cobb, M.D.

Cellular Injury and Adaptation Laboratory

Washington University School of Medicine

St. Louis, MO

Robert L. Danner, M.D.

Critical Care Medicine Department

Clinical Center

Bethesda, MD

Members

Peter Munson, Ph.D.

Center for Information Technology

National Institutes of Health

Bethesda, MD

Scott Somers, Ph.D.

National Institute of General Medical Sciences

National Institutes of Heath

Bethesda, MD

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Overview Agenda Speakers Hotel & Travel Registration Abstracts Exhibitors Contacts

SPONSORS The following NIH institutes, departments and centers are sponsoring this conference. Critical Care Medicine Department, Warren Grant Magnuson Clinical Center The National Institute of General Medical Sciences Office of Rare Diseases, Office of the SPONSORS Director National Human Genome Research Institute The National Cancer Institute National Institute of Arthritis and Musculoskeletal and Skin Diseases National Institute of Child Health and **Human Development** National Institute of Allergy and Infectious Diseases Microarray User Group

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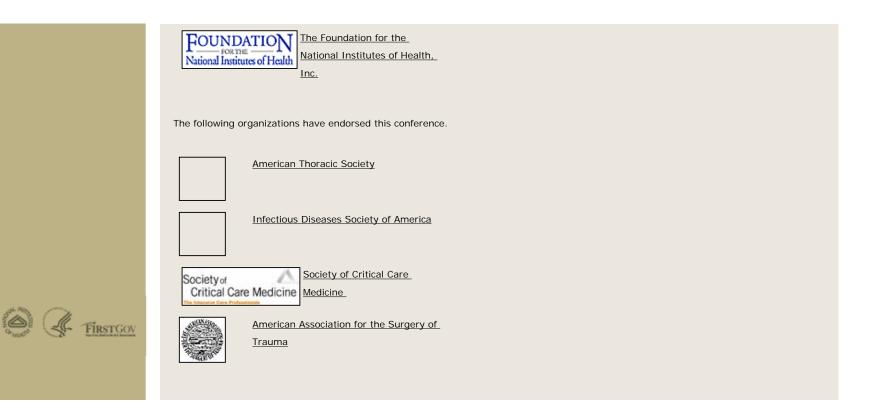
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Call for Abstracts



AGENDA	MONDAY, NOVEMBER	17, 200
MONDAY, NOVEMBER 17, 2003	8:45 AM	Opening remarks
TUESDAY, NOVEMBER 18, 2003	- 9:00 AM	After the Human Genome Project: Where Does Genomics Go From Here? Alan E. Guttmacher, M.D. National Institutes of Health
	9: 40 AM	Medical Implications of the Human Genome Project Christopher P. Austin, M.D. National Institutes of Health
	10: 20 AM	Break
	10:40 AM	The Diagnostic Proteome: Advances in Protein Diagnostics in Plasma N. Leigh Anderson, Ph.D. Plasma Proteome Institute
	11:20 AM	Proteomics: the Next Revolution in Molecular Medicine Lance Liotta, M.D. National Institutes of Health
	12:00 PM	Lunch
	1:00 PM	Poster viewing
	1:30 PM	SNPs, Haplotypes and Innate Immunity Stephen Chanock, M.D. National Institutes of Health
	2:10 PM	Innate Immune Sensing Pathways: How We Detect the Presence of Infection Bruce Alan Beutler, M.D. The Scripps Research Institute
	2:50 PM	Fever, Genes, and History: Natural Selection and the Systemic Autoinflammatory Diseases. Daniel Kastner, M.D., Ph.D. National Institutes of Health
	3:30 PM	Break
	3:50 PM	Oral Abstract Presentations
al Place and a	4:50 PM	Poster viewing and reception
FIRSTGOV	All day	Exhibits





AGENDA	TUESDAY, NOVEMBER 18, 20	03
MONDAY, NOVEMBER 17, 2003	8:45 AM	Oral Abstract Presentations
TUESDAY, NOVEMBER 18, 2003	9:00 AM	Pharmacogenomics of Acute Lymphoblastic Leukemia
		William E. Evans, Pharm.D.
		St. Jude Children's Research Hospital
	9:40 AM	The Neuroendocrine Response to the Severe Stress of Critical Illness
		Greet Van den Berghe M.D., Ph.D.
		University of Leuven
	10:20 AM	Break
	10.20 AW	Diedk
	10:40 AM	Mining a Gene Expression Database
		Peter Munson, Ph. D.
		National Institutes of Health
	11:20 AM	Predictions of Critical Systems (material failure, human parturition, earthquakes, financial
		crashes): Can the Complex System Approach be Useful to You?
		Didier Sornette, M.S., Ph.D.
		University of California
	12:00 PM	Lunch
	1:30 PM	Candidate Gene Approach to Acute Lung Injury
		Joe G. N. Garcia, M.D.
		Johns Hopkins University School of Medicine
	2:10 PM	Blood Leukocyte Gene Expression after LPS Administration to Human Volunteers and in
	2. 10 1 W	Traumatized Patients: Effect of RNA Isolation Methods
		Steven Calvano, Ph.D.
		The University of Medicine and Dentistry of New Jersey -Robert Wood Johnson Medical School

2:50 PM	Gene Expression Profiling in the Blood Compartment: The "Inflammation and Host Response to Injury Glue Grant" Experience Lyle L. Moldawer, Ph.D. University of Florida College of Medicine
3:30 PM	Break
3:50 PM	Oral Abstract Presentations

EIRSTGOV

N. Leigh Anderson, Ph.D.

Chief Executive Officer

Plasma Proteome Institute

Washington, DC

www.plasmaproteome.org

Dr. Anderson obtained his B.A. with honors in physics from Yale University and his Ph.D. in molecular biology from Cambridge University. Subsequently, he co-founded (with Dr. Norman Anderson) the Molecular Anatomy Program at the Argonne National Laboratory (Chicago).

Drs. N. Leigh Anderson and Norman Anderson together undertook the first systematic "proteomics" investigations of human plasma by 2-D electrophoresis. They further analyzed plasma protein micro heterogeneity, and the properties of plasma antibodies.

Currently, Dr. N. Leigh Anderson is the founder and Chief Executive Officer of the Plasma Proteome Institute, which aims to foster the comprehensive exploration of the proteins of human blood plasma (the plasma proteome) and the rapid application of novel protein measurements in clinical diagnostics.

Dr. Anderson was previously Chief Scientific Officer at Large Scale Biology Corporation, where he founded the division of proteomics in 1985, developed the first automated two-dimensional electrophoresis technology platform for proteomics research and pioneered a range of applications in drug discovery, toxicology, and surrogate markers. He also initiated a database of plasma proteins observed by 2-D electrophoresis and a collaboration with Pfizer that provided early direct evidence of the utility of multiple plasma protein marker panels in the study of inflammation and anti-inflammatory drug effects. More recently, Dr. Anderson initiated the plasma protein proteomics program at LSBC, which successfully developed immunosubtraction processes for removal of the 10+ most abundant plasma proteins and additional chromatographic fractionation processes for uncovering minor protein constituents.

Dr. Anderson holds 15 patents, has written one book and over 120 scientific publications, mainly in the areas of proteomics and its applications.

The Diagnostic Proteome: Advances in Protein Diagnostics in Plasma.

N. LEIGH ANDERSON, PH.D.

BRUCE ALAN BEUTLER, M.D.





CHRISTOPHER P. AUSTIN, M.D.

BRUCE ALAN BEUTLER, M.D.

STEVEN CALVANO, PH.D.

STEPHEN CHANOCK, M.D.

WILLIAM E. EVANS, PHARM.D.

JOSEPH G.N. GARCIA, M.D

ALAN E. GUTTMACHER, M.D.

DANIEL KASTNER, M.D., PH.D

LANCELIOTTA M.D. PH.D.

LYLE L. MOLDAWER, PH.D.

PETER I. MUNSON, PH.D.

DIDIER SORNETTE, M.S., PH.D

GREET VAN DEN BERGH





Christopher P. Austin, M.D.

Senior Advisor to the Director for Translational Research

National Human Genome Research Institute

National Institutes of Health

Bethesda, Maryland

www.genome.gov

Dr. Austin received his M.D. from Harvard Medical School in 1986 and did his residency in neurology and held a clinical fellowship at Massachusetts General Hospital, where he eventually became chief resident. From 1991 to 1996, he was a Research Fellow in Genetics at Harvard Medical School.

In his current position as Senior Advisor to the Director for Translational Research with the National Human Genome Research Institute,

Dr. Austin explores dissemination to academic investigators of the high-throughput technologies used in the private sector for deriving small molecule probes of biological pathways. His goal is to expand relationships with pharmaceutical and biotech companies, and focus on translating the data produced through the Human Genome Project into new therapeutic strategies.

From 1996 until taking his position with NIH, Dr. Austin worked at Merck Research Laboratories, most recently as the Director of Genomic Neuroscience in the Department of Neuroscience. He played a key role in Merck's pharmacogenomics program and initiated a drug development team that identified two molecular targets now being tested for the treatment of schizophrenia. Dr. Austin left Merck Research Laboratories in November, 2002.

"Medical Implications of the Human Genome Project."

Bruce Alan Beutler, M.D.

Professor

Department of Immunology

The Scripps Research Institute

La Jolla, California

www.scripps.edu

Dr. Beutler began his medical career as an intern in the Department of Medicine at the University of Texas. He then became a resident in its Department of Neurology. After a fellowship at The Rockefeller University, Dr. Beutler became an assistant professor there. From 1986 to 1991, Dr. Beutler was an assistant investigator at Howard Hughes Medical Institute in Dallas, Texas. He then was an assistant, associate, and full professor in the Department of Internal Medicine at U.T. Southwestern Medical Center. From 1991 to 2000, he was also an associate investigator at The Howard Hughes Medical Institute. Throughout his career, he has held various editorial and consulting appointments. Currently, Dr. Beutler is a professor at The Scripps Research Institute, Department of Immunology.

Dr. Beutler has published 90 research papers, 85 reviews and chapters, and two books. He has been issued three patents with four others pending. His current research interests are the role of cytokines in the inflammatory response and the molecular genetics of immune reactions.

Dr. Beutler obtained his B.A. from the University of California, San Diego (Revelle College) and his M.D. from the University of Chicago (Pritzker School of Medicine).

A member of various professional associations including the American Society for Hematology and the American Federation for Clinical Research, Dr. Beutler currently has funding support for six grants. He has spoken at 29 lectures and was a Finalist in the 2002 World Technology Award for Health and Medicine.



How the LPS receptor senses infection, causes shock, and triggers an adaptive immune response."



BRUCE ALAN BEUTLER, M.D.





BRUCE ALAN BEUTLER, M.D.

STEVEN CALVANO, PH.D.





Steven Calvano, Ph.D.

Associate Professor of Surgery

The University of Medicine and Dentistry of New Jersey -Robert Wood Johnson Medical School

Department of Surgery

Division of Surgical Sciences

New Brunswick, New Jersey

www.umdnj.edu

Dr. Calvano obtained his B.A. cum Laude from the University of Connecticut and his Ph.D. with Honors from the University of California. Currently, Dr. Calvano is Associate Professor of Surgery at UMDNJ-RWJMS.

Prior academic appointments in the Department of Surgery at Cornell University Medical College include the following: Staff Associate; Instructor; Assistant Professor; and Associate Professor. He is a member of the following professional organizations: American Association of Immunologists; Surgical Infection Society; American Burn Association; and the International Society for Burn Injuries.

Recipient of seven grants, Dr. Calvano is the author of numerous abstracts, refereed original articles in journals, and invited articles in journals and reviews.

Gene Expression in Blood Leukocytes After Endotoxin or Saline Administration to Human Volunteers.

CHRISTOPHER P. AUSTIN, M.I.

BRUCE ALAN BEUTLER, M.D.

STEVEN CALVANO, PH.D.

STEPHEN CHANOCK, M.D.

WILLIAM E. EVANS, PHARM.D

JOSEPH G.N. GARCIA, M.E

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LYLE L. MOLDAWER, PH.D.

PETER J. MUNSON, PH.D.

DIDIER SORNETTE, M.S., PH.D.

GREET VAN DEN BERGHE





Stephen Chanock, M.D.

Acting Director

Advanced Technology Center

National Cancer Institute

National Institutes of Health

Gaithersburg, Maryland

www.nci.nih.gov

Dr. Chanock received his M.D. from Harvard Medical School in 1983 and completed training in pediatrics, infectious diseases, and pediatric hematology/oncology at Children's Hospital in Boston and the Dana-Farber Cancer Institute.

Currently, Dr. Chanock is the Acting Director of the NCI Core Genotyping Facility (CGF), located at the Advanced Technology Center. He joined NCI in 1991, where he has been investigating the molecular, cellular, and clinical problems of infectious complications in patients with cancer and HIV infection. He also holds an appointment as a senior investigator in the Pediatric Oncology Branch of NCI's Center for Cancer Research.

"SNP's, Haplotypes and Innate Immunity." Abstracts

BRUCE ALAN BEUTLER, M.D.

WILLIAM E. EVANS, PHARM.D.







William E. Evans, Pharm.D.

Scientific Director, Deputy Director St. Jude Children's Research Hospital

www.stjude.org

Memphis, Tennessee

Dr. William Evans received his B.S. and Pharm. D. degrees from the University of Tennessee (1973, 1974) and spent a sabbatical year in Prof. Urs Meyer's laboratory at the University of Basel, Switzerland, in 1987-88.

Dr. Evans is Scientific Director and Executive Vice President of St. Jude Children's Research Hospital (SJCRH) and First Tennessee Bank Professor of Clinical Pharmacy, Pharmaceutics and Pediatrics at the University of Tennessee (UT) Colleges of Clinical Pharmacy and Medicine. He also is Deputy Director of SJCRH. As Scientific Director, he is the academic leader for all clinical and laboratory research at the hospital; he also oversees faculty recruitment, program development, budget planning, and space allocation.

From 1986-2002, Dr. Evans served as the Chair of Pharmaceutical Sciences at SJCRH and from 1983-1991 he was Chair of the Department of Clinical Pharmacy at UT.

For the past 25 years, Dr. Evans' research has focused on the pharmacodynamics and pharmacogenomics of anticancer agents, exploring genetic and biochemical mechanisms for inter-individual differences in drug disposition and response.

A recipient of numerous awards including two MERIT Awards from the NIH, the Leon Goldberg Award from ASCPT, and the ACCP Therapeutic Frontiers Lecture Award, Dr. Evans is an elected fellow of AAAS, AAPS, and ACCP and has held numerous elected offices on various organizations and boards.

Dr. Evans is on the Editorial Boards of seven scientific and professional journals, is US Editor of the journal Pharmacogenetics, and Editor of the textbook Applied Pharmacokinetics: Principles of Therapeutic Drug Monitoring. A member of the Board of Directors of the Memphis Area Chamber of Commerce, Dr. Evans has published more than 250 research articles and 30 book chapters and has been an invited speaker at over 250 universities, research institutes and international symposia, worldwide. He was elected to the Institute of Medicine, of the National Academy of Sciences, in 2002.

"Pharmacogenomics of Acute Lymphoblastic Leukemia."

Joseph G.N. Garcia, M.D.

"Dr. David Marine" Professor of Medicine

Director, Division of Pulmonary and Critical Care Medicine

Director, Center for Translational Respiratory Medicine

Johns Hopkins University School of Medicine

Baltimore, Maryland

www.hopkinsmedicine.org

Dr. Garcia received a B.S. in Biology in 1976 from the University of Dallas and his M.D. from the University of Texas Southwestern Medical School in 1980. From 1980-1983, he was an Intern and Resident at the University of Iowa Hospitals and Clinics Department of Internal Medicine in Iowa City, Iowa. From 1983-1985, Dr. Garcia was a Fellow at Albany Medical College Division of Pulmonary Diseases in Albany, N.Y.

Currently, Dr. Garcia is a "Dr. David Marine" Professor of Medicine (Endowed Chair) and a Professor of Biomedical Engineering at Johns Hopkins University School of Medicine. He is also a Professor of Environmental Health Science at Johns Hopkins University Bloomberg School of Public Health in Baltimore, MD.

Previous professional experience for Dr. Garcia includes his positions from 1984-1985 as Instructor, Department of Internal Medicine at Albany Medical College of Union University and from 1985-1988, Assistant Professor of Medicine at the University of Texas Health Center at Tyler, Tyler, TX. From 1988-1992, Dr. Garcia was Associate Professor of Medicine and from 1992-1998, a Professor of Medicine, Physiology and Biophysics at Indiana University School of Medicine. From 1994-1998, he was a Dr. Calvin H. English Professor of Medicine (Physiology/Biophysics) and an Endowed Chair at Indiana University School of Medicine.

Dr. Garcia is widely published with 186 articles, 17 book chapters, and 259 abstracts and has significant editorial activities. A member of numerous Professional Societies, Dr. Garcia organized several symposia and conferences and had been an invited speaker at numerous national and international conferences.

Dr. Garcia has been Principal Investigator and Co-Investigator for several grants relating to his specialty. He has also had significant teaching and mentoring responsibilities throughout his career.

BRUCE ALAN BEUTLER, M.D.

JOSEPH G.N. GARCIA, M.D..







"Candidate Gene Approach To Acute Lung Injury."

BRUCE ALAN BEUTLER, M.D.

ALAN E. GUTTMACHER, M.D.



Alan E. Guttmacher, M.D.

Deputy Director Senior Clinical Advisor to the Director National Human Genome Research Institute National Institutes of Health Bethesda, Maryland www.genome.gov

Dr. Guttmacher received an A.B. degree in 1972 from Harvard College and his M.D. from Harvard Medical School in 1981. From 1982 to 1985, Dr. Guttmacher was an intern and resident in pediatrics at Children's Hospital Boston. In 1985, he earned a two-year National Research Service Award from the U.S. Public Health Service as a fellow in medical genetics at Children's Hospital Boston and Harvard Medical School. Dr. Guttmacher is a Fellow of the American Academy of Pediatrics and a Fellow of the American College of Medical Genetics.

Currently, Dr. Guttmacher is the second Deputy Director of the National Human Genome Research Institute (NHGRI), the institution responsible for leading the Human Genome Project (HGP). As the NHGRI Deputy Director, Dr. Guttmacher plays a lead role in integrating genomics into medical practice, helps NHGRI develop new research tools to translate the findings of the HGP into new diagnostic tests and therapies, and oversees strategic planning for the institute and its impact on the field of genomics.

Dr. Guttmacher came to NHGRI in 1999 as the Senior Clinical Advisor to the Director. In 1999, he also co-founded a group called "Genetic Resources On the Web (GROW)", which works with organizations sponsoring genetic websites to ensure they contain high-quality information. GROW's membership includes approximately three dozen organizations.

Dr. Guttmacher also has played a critical role in guiding the National Coalition for Health Professional Education in Genetics (NCHPEG). This non-profit coalition promotes health-professional education and access to information about advances in human genetics. For its first three years, NCHPEG operated from within the genome institute. Dr. Guttmacher oversaw the maturation of NCHPEG into a freestanding entity with more than one hundred member organizations and its own executive director.

Dr. Guttmacher is the acting Director of the NHGRI Office of Policy, Planning, and Communications. Dr. Guttmacher also co-edited with Dr. Francis Collins a series about the application of advances in genomics to medical care for The New England Journal of Medicine. These two authors wrote the first and last articles in the series, which were published in Fall 2002.

Prior work experience for Dr. Guttmacher includes his role in 1987 as director of the Vermont Regional Genetics Center at the University of Vermont College of Medicine. While there, he launched a series of public health genetics programs. In addition, he directed the Vermont Cancer Center's Familial Cancer Program, the Vermont Newborn Screening Program, Vermont's only pediatric intensive care unit, and an NIH-supported initiative that was the nation's first statewide effort to involve the general public in discussion of the Human Genome Project's ethical, legal, and social implications. He also had a busy practice in clinical genetics, conducted research, and was a tenured associate professor of pediatrics and medicine at the University of Vermont College of Medicine.

"After the Human Genome Project: Where Does Genomics Go From Here?"

Registration



SPEAKER INFORMATION

BRUCE ALAN BEUTLER, M.D.

DANIEL KASTNER, M.D., PH.D.





Daniel Kastner, M.D., Ph.D.

Chief

Genetics and Genomics Branch

National Institute of Arthritis

and Musculoskeletal and Skin Diseases

National Institutes of Health

Bethesda, Maryland

www.niams.nih.gov

Dr. Kastner obtained his A.B. degree summa cum laude from Princeton University and completed the M.D., Ph.D. program at Baylor College of Medicine. While completing graduate studies with Dr. Robert R. Rich in the Department of Microbiology and Immunology, Dr. Kastner was the first to show cytotoxic T-lymphocytes directed against the MHC-associated Qa-1 molecule. Elected to the AOA, Dr. Kastner completed his M.D. with honor in 1982. He then completed his residency in Internal Medicine at Baylor and became Chief Resident in 1985.

Currently, Dr. Kastner is the Chief of the Genetics and Genomics Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institute of Health.

Dr. Kastner began his career at the NIH as a Rheumatogy Fellow, later shifting his research towards the genetic basis of human rheumatic disease. He was then appointed a Senior Investigator in the Arthritis and Rheumatism Branch of NIAMS and his laboratory work culminated in the identification of the FMF gene as a novel inflammatory regulator expressed in granulocytes. In 1999, his lab discovered that a dominantly inherited periodic fever syndrome similar to FMF is caused by mutations in the p55 TNF-receptor, a result that has led to the successful use of anti-TNF agents in this disorder. More recently, his group played a key role in the identification of mutations in CIAS1 associated with neonatal onset multisystem inflammatory disease (NOMID). In the past decade, Dr. Kastner's lab has also greatly contributed to understanding the genetic basis of cystinuria, the most common inherited form of kidney stones.

A member of several professional organizations including the American College of Rheumatology and the American Society for Clinical Investigation, Dr. Kastner is a recipient of a number of awards including the Lee C. Howley Prize for Research in Arthritis from the National Arthritis Foundation and the NIAMS Mentoring Award.

"Fever, Genes, and History: Natural Selection and the Systemic Autoinflammatory Diseases."

BRUCE ALAN BEUTLER, M.D.

LANCE LIOTTA, M.D., PH.D.





Lance Liotta, M.D., Ph.D.

Chief

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Bethesda, Maryland

www.nci.nih.gov

Dr. Lance Liotta received his undergraduate degree at Hiram College in 1969 and then completed an M.D./Ph.D. program at Case Western Reserve University in 1976. His Ph.D. is in biomedical engineering, with cancer metastasis as his Ph.D. thesis topic.

Dr. Liotta is Chief of the Laboratory of Pathology and Section on Tumor Invasion and Metastases for the National Cancer Institute in Bethesda, Maryland. He is also Chair of the NIH Radiation Safety Committee.

Prior work experience includes training as a resident in anatomic pathology at the NIH in the Laboratory of Pathology and becoming Chief of that laboratory in 1982.

Dr. Liotta is also the former Deputy Director for Intramural Research at the NIH.

"Proteomics The Next Revolution in Molecular Medicine."



Lyle L. Moldawer, Ph.D.

Professor of Surgery

University of Florida College of Medicine

Gainesville, Florida

www.med.ufl.edu

Dr. Moldawer received his Ph.D. in Experimental Medicine from the Medical Faculty at the University of Gothenburg, Gothenburg, Sweden in 1986. His research focuses on the pathophysiologic role of cytokines in the host response to acute and chronic inflammation.

Dr. Moldawer is presently a Professor of Surgery with tenure at the University of Florida College of Medicine, one of only a small number of Ph.D.s in the country with the academic rank of Full Professor in a Department of Surgery. Dr. Moldawer joined the Department of Surgery, University of Florida College of Medicine faculty in September, 1993 after serving seven years on the faculty of Cornell University Medical College initially as an Assistant and then Associate Professor of Surgery, and Associate Professor of Cell Biology and Anatomy.

Dr. Moldawer currently has 245 peer-reviewed publications. Since 1988, he has received continuous independent funding from the National Institutes of Health (NIH). In 1998, he was the recipient of the prestigious Merit Award from the National Institute of General Medical Sciences, extending his current NIH support through 2006.

Dr. Moldawer is the principal investigator on a NIH training grant to prepare surgical residents in training with a two-year research experience in molecular biology and gene therapy. Since 1988, he has trained 28 surgical residents in research methodologies.

Additionally, Dr. Moldawer is Co-Director of the Protein Analysis and Cell Biology Core, and a member of the Steering Committee, of a National Institute of General Medical Sciences Large Scale Collaborative Research Program (Glue Grant) entitled, "Inflammation and the Host Response to Injury", funded through 2006 to introduce functional genomics and high throughput proteomics into trauma and sepsis research.

He has sat on or currently sits on the editorial board of five journals, including the American Journal of Physiology, is an Associate Editor of the journal Shock and American Journal of Physiology, and is Section Editor of Current Opinion in Clinical Nutrition and Metabolic Care. A past member of the Metabolic Pathology Study Section of the NIH, Dr. Moldawer serves on special initial review groups for the National Institute of General Medical Sciences in the fields of graduate medical education, and burn and trauma physiology

BRUCE ALAN BEUTLER, M.D.

LYLE L. MOLDAWER, PH.D.





"Gene Expression Profiling in the Blood Compartment: The 'Glue Grant' Experience."

CHRISTOPHER P. AUSTIN, M.E.

BRUCE ALAN BEUTLER, M.D.

STEVEN CALVANO, PH.D.

STEPHEN CHANOCK, M.D.

WILLIAM E. EVANS, PHARM,D

JOSEPH G.N. GARCIA, M.D

ALAN E. GUTTMACHER, M.D.

DANIEL KASTNER, M.D., PH.D.

LANCE LIOTTA, M.D., PH.D.

LYLE L. MOLDAWER, PH.D.

PETER J. MUNSON, PH.D.

DIDIER SORNETTE, M.S., PH.D.

GREET VAN DEN BERGH





Peter J. Munson, Ph.D.

Chief of Mathematical and Statistical Computing Laboratory

Center for Information Technology

National Institutes of Health

Bethesda, Maryland

www.cit.nih.gov

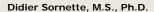
Dr. Munson heads the Mathematical and Statistical Computing Laboratory within the Division of Computational Biosciences, Center for Information Technology, at the National Institutes of Health. In addition to pursuing its research mission, his group acts as a resource for the NIH Intramural Research Program, with special emphasis on mathematical physics, mathematical modeling, statistics and bioinformatics. Dr. Munson's group has led the development and application of statistical and computational methods to the analysis of microarray-based experiments. His lab has developed software packages (P-SCAN, F-SCAN) for the analysis of microarray images and a high-throughput analysis pipeline (A-SCAN) for Affymetrix-based array experiments. Dr. Munson has served in the Center for Information Technology and earlier at the National Institute of Child Health. He received his bachelor's degree from St. Olaf College, master's from the University of Wisconsin, Madison, and Ph.D. in mathematical statistics from American University. He has authored more than 100 publications on the application of statistical methodology and mathematical modeling to problems in endocrinology, pharmacology, oncology, protein structure prediction and bioinformatics.

"Mining a Gene Expression

Database"

BRUCE ALAN BEUTLER, M.D.

DIDIER SORNETTE, M.S., PH.D.



Professor of Geophysics

Institute of Geophysics and Planetary Physics

and Department of Earth and Space Science

University of California

Los Angeles, California

www.ess.ucla.edu

Dr. Didier Sornette received his M.S. in Physical Sciences from Ecole Normale Superieure in 1981 and completed his Master thesis on Statistical Physic of membranes at the University of Nice in 1981. He was a Research Scientist of the CNRS (French National Center for Scientific Research) from 1981 until 1990. In 1985, he completed his Ph.D. on the Statistical Physics of Interfaces at the University of Nice, France.

Dr. Sornette is presently a Professor of Geophysics at the Institute of Geophysics and Planetary Physics and the Department of Earth and Space Science at the University of California.

Prior academic work experience includes Post-Doctoral work in the Condensed Matter Laboratory of Prof. P.G. de Gennes at College de France from 1985-1986. Dr. Sornette was also a Visiting Professor in the following locations: Canberra, Australia; Ecole Polytechnique, Paris; and Santa Barbara, California. Since October, 1990, Dr. Sornette has been a Research Director at CNRS, France. From 1996 until June, 1999, Dr. Sornette was a Professor-in-Residence part-time at the Department of Earth and Space Science and at the Institute of Geophysics and Planetary Physics, UCLA.

Dr. Sornette's prior industrial experience includes the following: Director of Research in the X-RS research and development company in Orsay, France from 1988-1995; Scientific Advisor of the Technical Director of Thomson-Marconi Sonar company in Nice-Sophia Antipolis Technopolis, France from 1984-1996; and Advisor of aerospace industrial companies, banks, investment, and reinsurance companies.

A recipient of numerous awards including the 2000 Research McDonnell award (Studying Complex Systems, the Scientific Prediction of Crises) and the Risques-Les Echos prize in 2002 (Predictability of catastrophic events: material rupture, earthquakes, turbulence, financial crashes and human birth), Dr. Sornette on the editorial boards of several scientific and professional journals.

Dr. Sornette is the author and coauthor of more than 300 research papers in refereed journal and more than 120 papers in books and conferences proceedings, editor of two proceedings of two international conferences, author of two books, and has spoken more than 200 times at international conferences and Universities worldwide. He also directed nine completed Ph. D. theses and directed eighteen postdoctorates.

"Predictions of Critical Systems (material failure, human parturition, earthquakes, financial crashes): Can the Complex System Approach be Useful to You?"



Abstracts

CHRISTOPHER P. AUSTIN, M.D.

BRUCE ALAN BEUTLER, M.D.

STEVEN CALVANO, PH.D.

STEPHEN CHANOCK, M.D.

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PETER I. MUNSON, PH.D.

DIDIER SORNETTE, M.S., PH.D.

GREET VAN DEN BERGHE M.D., PH.D.





Greet Van den Berghe M.D., Ph.D.

Head

Department of Intensive Care Medicine

University Hospital Gasthuisberg

University of Leuven

Leuven, Belgium

Dr. Van den Berghe received her M.D. from the University of Leuven. From 1985-1989, she completed Training in Anaesthesiology at the University of Leuven and then completed a postgraduate course in Biostatistics from 1988-1989. From 1989-1991, she completed training in Intensive Care Medicine at the University of Leuven and in 1994 completed her Ph.D. there; Dr. Van den Berghe's Ph.D. thesis was "Dopamine and Pituitary Hormones in Critical Illness."

Currently, Dr. Van den Berghe is Chair of the Department of Intensive Care Medicine of the University Hospital Gasthuisberg, University of Leuven, Belgium. Her current academic position is Professor Intensive Care Medicine, University of Leuven (1995, 1998, 2001). Dr. Van den Berghe is also Clinical Research Investigator for the Belgian Fund for Scientific Research and a Member of the Belgian Royal Academy of Medicine and the Ethical Committee of the Belgian Ministry of Agriculture. Since February, 2002, Dr. Van den Berghe has been the K.U. Leuven-Novo Nordisk Chair of Research on Insulin in Critical Illness.

Author of numerous abstracts, book chapters, articles in scientific publications, and University Press' Dopamine and Pituitary Hormones in Critical Illness, Dr. Van den Berghe has reviewed more than 30 manuscripts per year for International Journals and presented at more than 100 International Meetings. Dr. Van den Berghe has received 18 Research grants and is the recipient of 19 scientific awards including, most recently, The Menarini Award for Diabetology 2003. She has supervised two Ph.D. Theses and been on the Jury membership of three other Ph.D. theses.

Dr. Van den Berghe organized the following two scientific meetings: International Symposium on Intensive Care Medicine, Leuven (November 20, 1998) and the Symposium at the occasion of the retirement of Prof. Dr. Peter Lauwers, Leuven (September 7, 2002).

"The Neuroendocrine
Response to the Severe
Stress of Critical Illness."

Overview Agenda Speakers Hotel & Travel Registration Abstracts Exhibitors Contacts

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A block of rooms has been reserved for symposium attendees at several hotels in the Bethesda area for the nights of November 16-17, 2003. You are encouraged to make your hotel reservation as soon as possible to obtain the special rate of \$150 per night plus tax (12%). Please note that each hotel has a different cutoff date (see below). After these dates, the hotels will accept reservations on a space available basis only at the prevailing rate.

Four Points Sheraton

8400 Wisconsin Avenue

Bethesda, Maryland 20814

301.654.1000

301.654.0751, guest fax

Location:

It is a five-minute walk from the hotel to the Natcher Conference Center. Shuttle service to Natcher Conference Center is available Monday and Tuesday at 7:30 a.m. and 8:00 a.m. The shuttle has limited seating, so it is first come, first served.

Accommodation:

The standard rooms have large working desks and a sitting area. All rooms offer data port, voicemail, and access to a fitness facility and restaurant.

Check-in time: 3:00 p.m. Check-out time: Noon

Rates and Reservations:

Rates: \$150.00 per single or double room per night

Daily Parking fee: \$7.00

Cutoff date: November 2, 2003

Reservations: call 301.941.2719, 301.986.1715, fax

Reservation Name: 1108 Functional Genomics of Critical Illness and Injury

Holiday Inn Select Bethesda

8120 Wisconsin Avenue

Bethesda, Maryland 20814

301.652.2000

301.652.3806, guest fax

Location:

The hotel is .5 miles from NIH and is a 15-minute walk to Natcher Conference Center. Hotel shuttle service is available hourly to NIH.

Accommodation:

The standard rooms have been newly renovated and include data port, voicemail, and access to the health club and restaurant.

Check-in time: 4:00 p.m. Check-out time: 12:00 p.m.

Rates and Reservations:

Rates: \$150.00 per single or double room per night

Daily Parking Fee: \$ 10.00 Cutoff date: October 24, 2003

Reservations: call 1.877.888.3001, 301.652.2000

Reservation Name: Functional Genomics of Critical Illness and Injury

Bethesda Marriott

5151 Pooks Hill Road

Bethesda, Maryland 20814

301.897.9400, phone

301.897.0192, guest fax

Location:

The hotel is 1.5 miles from NIH. Shuttle service to Natcher Conference Center is available every 30 minutes.

Accommodation:

The standard rooms have a work desk, speakerphone, data port and voice mail, and access to an indoor pool, health club, and restaurant.

Check-in time: 4:00 p.m.
Check-out time: 12:00 p.m.

Rates and Reservations:

Rates: \$150.00 per single or double room per night.

Daily Parking Fee: no fee Cutoff date: October 20, 2003

Reservations: call 1.800.228.9290, 301.897.9400

Reservation Name: Functional Genomics of Critical Illness and Injury





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Take the Red Line toward Shady Grove or Grosvernor. Exit at the Medical Center Metro Station. At the top of the escalators, take the stairs or ramp to your left and follow the path to the Natcher Conference Center. For more METRO information, please visit www.wmata.com



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ENTRANCE AND EXITS AT THE NATIONAL INSTITUTES OF HEALTH

All visitors must use the following two entrances:

- 1- Rockville Pike (Rte. 355) and South Drive
- 2- Old Georgetown Road and Center Drive

All visitor vehicles, including taxicabs, hotel and airport shuttles, will be inspected before being allowed on campus. Visitors will be asked to show a photo ID and state the purpose of their visit.

Be sure to allow extra time for this vehicle inspection procedure.



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DRIVING DIRECTIONS TO THE NATIONAL INSTITUTES OF HEALTH

From Baltimore and All Points North of Washington, DC

Take I-95 south toward Washington, DC. At I-495 (Capital Beltway), head west toward Silver Spring/Bethesda. From the Beltway (I-495), take Exit 34, which is Rt. 355 (Wisconsin Ave./Rockville Pike) and head south toward Washington/Bethesda. At the fourth traffic light, turn right onto South Drive and bear right to the vehicle inspection area.

From Virginia and All Points South of Washington, DC

Take I-95 north toward Washington, DC. At I-495 (Capital Beltway), head north toward Silver Spring/Bethesda. From the Beltway (I-495), take Exit 34, which is Rt. 355 (Wisconsin Ave./Rockville Pike) and head south toward Washington/Bethesda. At the fourth traffic light, turn right onto South Drive and bear right to the vehicle inspection area.

From Ronald Reagan National Airport

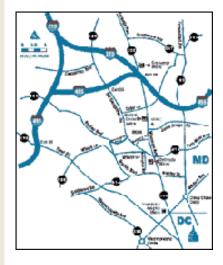
Head North on the George Washington Parkway for approximately 5 miles. Exit onto I-495 (Capital Beltway), heading north to Maryland. From the Beltway (I-495), take Exit 34, which is Rt. 355 (Wisconsin Ave./Rockville Pike) and head South toward Washington/Bethesda. At the fourth traffic light, turn right onto South Drive and bear right to the vehicle inspection area.

From Baltimore-Washington International Airport (BWI)

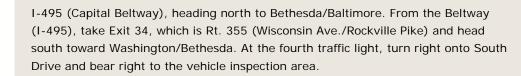
Take the Baltimore-Washington Parkway south toward Washington, DC. At I-495 (Capital Beltway), head west toward Silver Spring/Bethesda. From the Beltway (I-495), take Exit 34, which is Rt. 355 (Wisconsin Ave./Rockville Pike) and head south toward Washington/Bethesda. At the fourth traffic light, turn right onto South Drive and bear right to the vehicle inspection area.

From Dulles International Airport

Head east on the Dulles Airport Access Road for approximately 13 miles. Exit onto



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Parking on the NIH campus is extremely limited. There is a small paid parking lot next to the Natcher Conference Center. The parking fee is \$2 per hour for the first three hours or \$12 per day.



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National Institutes of Health

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Natcher Conference Center

All non-federal employees will need to pass through Security. Plan to have two forms of identification including a picture identification. Visitors may be required to pass through a metal detector and may have their bags, backpacks, or purses inspected or x-rayed as they enter Natcher Conference Center. Meeting participants may want to leave extra bags or personal materials at their hotel to minimize the time needed for inspection.

Please allow for an additional 20 minutes to pass through Natcher Conference Center Security.

GUIDELINES FOR SUBMISSION

GUIDELINES FOR SUBMISSION

ON-LINE SUBMISSION

The Organizing Committee invites you to submit an abstract of your scientific research to be considered for an oral or poster presentation at the Second Annual Symposium on the Functional Genomics of Critical Illness and Injury, November 17- 18, 2003. The deadline for submission is Friday, October 17, 2003. Notice of acceptance will be sent by Friday, October 31, 2003. An abstract booklet will be prepared and handed out to all attendees.

PLEASE NOTE: Conference registration is required for everyone submitting abstracts (see registration page).

All abstracts are to be submitted electronically through the following On-Line Abstract Submission form.

Abstract Title: An abstract must have a short, specific title that indicates the nature of the investigation.

Contact/Presenter name: Include information for the presenting author, who should receive all correspondence concerning this abstract. All submissions should include mailing address, telephone, and e-mail address.

Author(s): List all authors of the abstract. For each author supply the first initial and last name.

Affiliation(s): List all affiliations with city, state, and country.

Key words: Provide three key words that best describe the topic or topics addressed in the abstract.

Abstract text: Upload the body of your text. Abstracts must be submitted in Microsoft Word. The abstract should have four clearly identifiable components: Background, Methods, Results, and Conclusion. You may use special Greek or mathematical characters in your abstract as well as charts and images. Text, charts, and images of your abstract must fit within a 3 inch by 5 inch block. Text must not exceed 250 words (excluding title and author(s)). The abstract must be submitted in Times New Roman font, 12 pitch and single-spaced.

Source of funding: List primary and secondary sources.

Financial Disclosure: Authors of scientific oral or poster presentations who have entered into a financial relationship with sponsoring companies or organizations about whose product or services they are reporting must include a disclosure statement at the end of their abstracts, e.g., "Research supported by ACME Pharmaceuticals." It is

IMPORTANT DATES

October 17, 2003

Deadline for abstract submission

October 31, 2003

Notification of oral and poster presentations

November 17- 18, 2003

Conference: Functional

Genomics of Critical Illness
and Injury

recognized that much scientific research is supported by organizations that have a commercial interest in the results of the research. The disclosure policy is not intended to discourage such support or restrict the dissemination of the research, but rather to permit members of the audience to form their own judgments about the research with the full disclosure of the facts.

full disclosure of the facts. **On-Line Submission** Please complete all fields. Abstract title: Contact/presenter name: (Ex: A. Smith) Address: Telephone: (Ex: 123-456-7890) E-mail: Affliliation: If selected, will you give an oral presentation? Yes No Author(s): Ex: A. Smith (1) J. Jones (2) P. Brown (1) Affiliation(s): List all affiliation(s) and assign number to authors. Ex: 1- ABC Hospital 2- XYZ Medial Center

Key words:

Three key words

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	Primary and secondary sources	Secondary		
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SPEAKER INFORMATION

Exhibition date: November 17, 2003

Conference dates: November 17 - 18, 2003

Location: Atrium Level

Natcher Conference Center

National Institutes of Health

Exhibit Fee: Bethesda, Maryland

\$500

Exhibitor Information, please view and print the $\underline{\text{Prospectus}}$ in PDF format.

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If you have any questions regarding logistics or registration, please contact:

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Donna Moss

Strategic Results

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Baltimore, MD 21210

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donna@strategicresults.com





N. Leigh Anderson, Ph.D.

Chief Executive

Officer

Plasma Proteome

Institute

Washington, DC

www.plasmaproteome.

org

"The Diagnostic Proteome: Advances in Protein Diagnostics in Plasma."

The human plasma proteome holds the promise of a revolution in disease diagnosis and therapeutic monitoring, provided that major challenges in proteomics can be addressed. Plasma represents the largest and deepest version of the human proteome present in one sample: it contains all tissue proteins (as leakage markers) plus very numerous immunoglobulin sequences, and it has an extraordinary dynamic range (more than 10 orders of magnitude in concentration separate albumin and the rarest proteins now measured clinically). While almost 150 proteins are measured clinically in plasma, the rate of introduction of new individual protein tests approved by the FDA has paradoxically declined in the last 10 years. Recent results in proteomics indicate that patterns of change across panels of proteins will overcome the shortfall in new individual markers. Fortunately, the in vitro diagnostics industry provides a mature technology base for sensitive (<10pg/ml), accurate (CV<5%) protein assays, and major advances are being made in multivariate data interpretation (many shared with the DNA microarray field). The stage is thus set for important improvements in disease diagnosis and management.

N. Leigh Anderson, Ph.D.





Christopher P. Austin, M.D.

Senior Advisor to the

Director for

Translational

Research

National Human

Genome Research

Institute

National Institutes

of Health

Bethesda, Maryland

www.genome.gov





Medical Implications of the Human Genome Project

With the completion of the Human Genome Project has come the imperative to translate the sequence into tangible improvements in human health. These advances will emerge in three general areas: improved understanding of the molecular pathogenesis of disease, improved diagnosis and treatment based on genetic information, and new therapeutics based on genomic insights. These developments, and their expected timelines, will be discussed. Realization of the genome's promise for medicine will require new paradigms in biological research and drug discovery, and will rely on increased physician knowledge of genetic principles applied to common diseases.

Christopher P. Austin, M.D.

Bruce Alan Beutler, M.D.

Professor

Department of

Immunology

The Scripps Research

Institute

La Jolla, California

www.scripps.edu

Innate Immune Sensing Pathways: How We Detect the Presence of Infection

Germ line mutations have revealed the principal pathways by which the host senses infectious organisms. This awareness translates into an effective microbicidal response on the part of innate immune cells (macrophages, neutrophils), and also into activation of the adaptive immune response (an adjuvant effect). Initial insight into the nature of the primary molecular sensors grew from positional cloning of the Lps locus in mice, which was known to govern all cellular responses to lipopolysaccharide (LPS). Lps was revealed as TIr4, and a single mutation in TLR4, a membrane protein with homology to the Toll receptor of Drosophila, was capable of abolishing LPS sensing. TLR4 was found to be one member of a family of paralogs that each sense different components of microbes. Subsequently, targeted deletion of other paralogs of the family was found to disrupt sensing of peptidoglycan, bacterial lipopeptides, unmethylated DNA, and dsRNA. The biochemical pathways through which TLRs receive and transmit signals have been dissected by forward genetic analysis. Germ line mutations are created at random using a chemical mutagen, and mice with selective defects of innate immunity are identified by a series of screening assays. Lps2, a germ line mutant that disrupted LPS and dsRNA sensing, proved that TLRs 3 and 4 share a common adapter protein. We identified this adapter as Trif, or Ticam-1, one of five proteins known to carry signals from the TLRs. We demonstrated that it is responsible for My D88-independent LPS signaling, and, specifically, that it mediates the adjuvant effect of LPS, which depends in turn upon type I interferon signaling. We have also identified mutations that disrupt peptidoglycan sensing, and a mutation that interferes with dsRNA detection through a pathway extrinsic to the TLR3 -> Trif axis. These mutations have greatly expanded our understanding of how microbes trigger an immune response, and have also shed light on the phenomenon of sepsis insofar as the biochemical pathways



that cause sepsis are identical to those that sense microbial infection.

Bruce Alan Beutler, M.D.

Steven Calvano, Ph.

Associate Professor
of Surgery
The University of
Medicine and
Dentistry of New
Jersey -Robert Wood
Johnson Medical
School
Department of
Surgery
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New Brunswick,
New Jersey
www.umdnj.edu

Blood Leukocyte Gene Expression after LPS Administration to Human Volunteers and in Traumatized Patients: Effect of RNA Isolation Methods1

A major aim of the Inflammation and Host Response to Injury Large-Scale Collaborative Program funded by NIGMS is to identify the gene expression profiles of blood leukocytes in trauma and burn patients and to use these profiles to develop predictive algorithms for outcome variables. As a prelude to studies in actual patients, the human endotoxin model was used to evaluate the equivalency of three techniques to isolate blood leukocytes and to further characterize the transcriptomic elements that regulate systemic inflammation. These gene expression patterns were then compared to those from a group of trauma and burn patients. Human volunteers were administered LPS (n=4, 2 ng/kg IV bolus) or saline (n=2). At 0, 2, 4, 6, 9, and 24 hrs after LPS was given, blood leukocytes were isolated by PAXGene‰ (PG), a buffy coat (BC) isolation, and a whole blood lysis protocol (LY). Purified total RNA was used to generate cRNA which was hybridized to Affymetrix GeneChips‰ (U133A & U133B; 22,000 probe sets each). Leukocytes from patients with traumatic or burn injuries (n = 8) were prepared by the same three methods, and gene expression profiles were generated as above. In an unsupervised hierarchical clustering analysis, gene expression for the time points of the two control subjects (no LPS) clustered with the expression profiles at the 0 and 24 hr. time points of the subjects who received LPS. Gene expression profiling from the subjects receiving LPS showed a temporal change in expression that was dependent on the leukocyte isolation method. Using a supervised analysis trained on time, analysis of variance identified probe sets significant at p < 0.001. LY identified 5,844 significant probe sets, BC 3,698 probe sets, and PAX 2,630 probe sets. Hierarchical clustering of the data from the trauma/burn patients indicated a major node between PAX versus BC and LY. Further, concurrent analysis of the saline-treated controls, LPS-treated volunteers, and the trauma/burn patients revealed a distinct cluster for six of the eight trauma/burn patients. The remaining two patients clustered with the controls. We conclude: (1) the three blood leukocyte isolation methods tested are not equivalent, (2) the response by blood leukocytes to LPS administration represents substantial reprioritization in gene expression, and (3) there are unique as well as common gene expression patterns in LPS-induced systemic inflammation in comparison with traumatic injury.

Steven E. Calvano, Ph.D.

1 Supported by NIGMS grant U54 GM-62119

William E. Evans, Pharm.D.

Scientific Director,
Deputy Director
St. Jude Children's
Research Hospital
Memphis, Tennessee
www.stjude.org

Pharmcogenomics of Acute Lymphoblastic Leukemia

Acute lymphoblastic leukemia (ALL) comprises a number of genetic subtypes that are created by non-random chromosomal translocations producing aberrant gene fusions. Specific genetic subtypes having significantly different prognoses (Pui and Evans, NEJM, 1998). We have shown that the pattern of gene expression in ALL blasts, prior to treatment, discriminates among the major genetic and lineage subtypes of childhood ALL, and that gene expression profiles (U95A) are able to identify patients who have a high risk of treatment failure (Yeoh et al., Cancer Cell, 2002). More recently, we have taken a genome-wide approach (U95A) to determine whether there are non-random changes in gene expression following treatment with individual antileukemic agents or combinations, and whether gene expression differs according to the specific treatment given (Cheok et al., Nature Genetics, 2003). This approach has revealed distinct treatment-specific changes in gene expression after in vivo exposure to anticancer agents, and established that leukemia cells of different genetic or lineage subtypes share common pathways of genomic response to the same medications. To extend this work, we are assessing genomic determinants of the intracellular disposition of antileukemic agents, which has revealed gene expression profiles (U95A) that discriminate the level of intracellular accumulation of methotrexate polyglutamates (MTXPG) after in vivo high-dose MTX treatment. This assessment revealed genes that discriminated patients whose ALL cells accumulated high versus low MTXPG concentrations, providing new insight into the genomic determinants of the intracellular disposition of this agent. In collaboration with the Rotterdam group at Sophia, we have used gene expression profiling (U133A) of leukemia cells to identify genes that discriminate ALL cells that exhibit in vitro sensitivity versus resistance (lowest third versus highest third for LC50 in MTT assay) to L-asparaginase, daunorubicin, vincristine and prednisolone. Finally, we have used a similar approach to identify genomic differences in patients whose ALL cells have high versus low rates of de novo purine synthesis, a target of some antileukemic agents. Collectively, these studies and those by others illustrate the potential of gene expression profiling of primary cancer cells to illuminate genomic determinants of treatment response, providing new insights for optimizing cancer chemotherapy and developing new agents to augment current treatment.

William E. Evans, Pharm.D.

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Candidate Gene Approach to Acute Lung Injury

Acute lung injury (ALI), a cause of acute respiratory failure (sepsis, pneumonia or gastric aspiration, etc.), invariably requires assisted ventilation with positive pressure. Although ventilator-associated lung injury (VALI) significantly contributes to respiratory failure, the molecular pathophysiology is incompletely defined and novel therapies are not available. Furthermore, the genetic basis for this susceptibility and enhanced ALI severity is unknown. Genomic technologies provide the opportunity not only to characterize pulmonary responses to VALI with increased sensitivity and clarity but also to identify new molecular targets for potential therapy. We have conducted comprehensive genomic studies of human and animal models of ALI with rigorous phenotypic characterization in order to employ a candidate gene approach with differential gene and protein expression studies. This approach has led to the generation of an ALI candidate gene list including novel genes not previously associated with ALI. We have validated the physiological importance of these genes in a large cohort of well-phenotyped patients with ALI, using functional genomics and proteomic approaches with characterization of potentially important polymorphisms. These data provide new insight into the pathogenesis of ALI and the molecular basis for rational mechanical ventilation strategies, and help elucidate the relationship of mechanical stress to the activation of pathological gene expression in genetically susceptible patients.

Joe Garcia, M.D.

Supported by the NHLBI HopGene Program in Genomic Applications (HL 66618) and a Specialized Center for Clinical Oriented Research award (SCCOR) (HL 073994)

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Gene Expression Profiling in the Blood Compartment: The "Inflammation and Host Response to Injury Glue Grant" Experience

Using DNA microarrays to investigate gene expression patterns in whole blood from critically ill patients may provide insights into the nature of the immunoinflammatory response. As part of an NIGMS-funded Large Scale Collaborative Research Program, one of our goals has been to use DNA microarray analyses to identify apparent gene expression patterns in whole blood that may predict outcome from serious trauma or burn injury. We hope to further advance the basic understanding of the innate immune and immunoinflammatory responses in hospitalized patients by identifying leukocyte gene expression patterns that define a common response to traumatic and burn injury. Unfortunately, at present little is known about the role of sample preparation in gene expression profiles from healthy subjects and critically ill patients. Over the past 24 months, the program has examined the equivalency of gene expression profiles from ex vivo Staphylococcus enterotoxin B (SEB) stimulated and unstimulated human blood, from healthy, human volunteers receiving IV administration of bacterial endotoxin, and from severely traumatized patients. Several different RNA isolation methods from whole blood and isolated leukocyte populations have been employed. Total RNA has been isolated from buffy coat, enriched blood T cell or monocyte populations, and with the PAXgene™ blood collection system. Biotin-labeled cRNA was subsequently hybridized to Affymetrix GeneChips™. Hierarchical clustering and principal component analysis revealed that the primary differentiating parameter for gene expression in all of these populations was the RNA isolation method. The intraclass correlation--a measure of signal to noise ratio--of the difference between stimulated and unstimulated blood was lower with PAXgene™ derived samples than with buffy coat isolations. Gene expression patterns obtained from T-cell and monocyte enriched populations clustered more closely with themselves than they did with the other cell enriched populations or with expression patterns obtained from buffy coat or PAXgene™-derived samples. We conclude that RNA isolation techniques influence apparent gene expression profiles from whole blood.

Lyle L. Moldawer, Ph.D.





Peter J. Munson, Ph. D.

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Mining a Gene Expression Database

The now widespread interest in gene expression is motivated by the promise of important new findings in the context of disease or basic biology research. Because of cost constraints, most designed studies are relatively small, involving from 2 to 100 chips. Pooling results of studies allows one to compare expression across potentially thousands of conditions, with greater promise of additional insights. The NIHLIMS database houses data from about 30 ongoing studies at NIH comprising about 1500 Affymetrix chips, and provides a platform for testing data-mining approaches.

Serious challenges to comparability can be addressed in part with appropriate data normalization. We have investigated factors which distinguish patterns of expression. In addition to many technical factors, the cell or tissue type from which mRNA is prepared seems to be a primary source of variability, thus allowing identification of tissue-specific genes. Limited demographic information may be available, permitting, for example, the determination of gender-specific gene expression patterns. In one particular study, the identification of tissue-specific genes in human was compared to tissue-specific genes for the homologous tissue in rodent. This approach enabled an evolutionary comparison of the relevant expression mechanisms.

We will discuss several of the statistical techniques needed to compare data across studies, and present a list of challenges now facing data miners.Peter

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Predictions of Critical Systems (material failure, human parturition, earthquakes, financial crashes): Can the Complex System Approach be Useful to You?

Most out-of-equilibrium systems in the natural and social sciences exhibit an intermittent dynamics punctuated by rare but extreme crises. These are characteristic properties of the living realm and in particular of human health. Proceeding from interdisciplinary research using the complex system approach, we present empirical evidence suggesting that such crises are often endogenous and result from a cooperative self-organization of the system coupled with its environment. Drawing on ideas and tools from the theory of critical phenomena in statistical physics and from artificial/computational intelligence, we introduce a new framework for the prediction of such crises. We show that it is also possible to distinguish between their endogenous and exogenous origins and to unravel their interplay. Concrete applications include the prediction of material ruptures, earthquakes, financial market crashes, human parturition, commercial sales on amazon.com, etc.

Didier Sornette, M.S., Ph.D.





Greet Van den Berghe M.D., Ph.D.

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The Nneuroendocrine Response to the Severe Stress of Critical Illness

Sepsis, excessive inflammation, multiple organ failure and weakness prolong the need for intensive care in critically ill patients. Furthermore, the risk of death is high and hypercatabolism is present in the prolonged critically ill patient. The initial "adaptive" neuroendocrine response to critical illness illness consists primarily of activated anterior pituitary function. In the chronic phase of critical illness, a uniformly reduced pulsatile secretion of anterior pituitary hormones has been observed, impairing the function of whereby impaired function of target organs. A reduced availability of thyrotropin (TSH)-releasing hormone (TRH), gonadotropin (LH)-releasing hormone (GnRH), the endogenous ligand of the growth hormone (GH)-releasing peptide (GHRP) receptor (ghrelin) and, in very long-stay critically ill men also of GH-releasing hormone (GHRH), appear to beinferrentially appears involved. Pulsatile secretion of GH, TSH and LH can be re-amplified by relevant combinations of releasing factors which also substantially increases circulating levels of insulin-like growth factor (IGF)-I, GH-dependent IGF-binding proteins, thyroxine (T4), triiodothyronine (T3) and testosterone. Anabolism is only evoked when GH-secretagogues and TRH and perhaps also GnRH are administered together; whereas the effect of single hormone treatment is minor and accompanied by side effects. A remarkable observation was that a high serum concentration of IGF-binding protein 1 predicts death in the ICU. This observation challenged the classical dogma of adaptive hyperglycemia during critical illness. In a large prospective randomized clinical study showed, it was shown that ICU mortality and morbidity areis dramatically reduced with strict normalization of glycemia using exogenous insulin infusion. Further study indicatesd that glycemic control, rather than the amount of insulin infused per se, determinesd the beneficial effects on outcome. Ongoing studies are analyzsing the importance of the effect of intensive insulin therapy on lipid metabolism, other endocrine abnormalities, immune function, inflammation and coagulation in explaining the life-saving effect of this intervention. In conclusion, the new concept of reduced stimulation of pituitary function in prolonged critically ill patients opens new therapeutic perspectives reversingto reverse the paradoxical "'wasting syndrome."' Furthermore, but that maintenance of strict normoglycemia with insulin is crucial to also increasinge the chances of survival of these patients.

Greet G. Van den Berghe M.D., Ph.D.

FUNCTIONAL GENOMICS OF CRITICAL ILLNESS AND INJURY System Map Red Line • Glenmont to Shady Grove Orange Line • New Carrollton to Vienna/Fairfax-GMU Legend Orange Line • New Carroliton to Viennar an inacomine Blue Line • Franconia-Springfield to Largo Town Center Plaining Haller Haller Commuter Rail O Glenmont 🕾 0000000 0000





















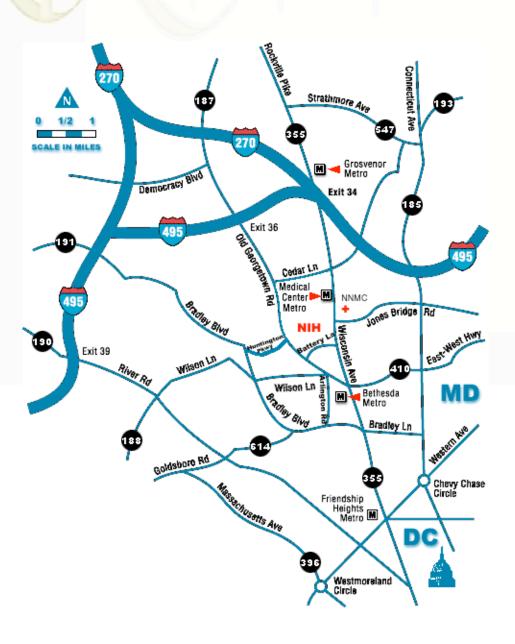


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Second Annual Symposium: Functional Genomics of Critical Illness and Injury

Exhibition Date: November 17, 2003

Conference Dates: November 17 – 18, 2003

Natcher Conference Center National Institutes of Health Bethesda, Maryland

Neither NIH nor the Clinical Center endorse or imply endorsement of the Exhibitors [vendors], their products or services.



Dear Exhibitor

I am pleased to invite you to exhibit at the Second Annual Symposium on the Functional Genomics of Critical Illness and Injury to be held on Monday, November 17-18, 2003, at the Natcher Conference Center, National Institutes of Health, Bethesda, Maryland.

The 2003 Symposium and first-time exhibit promises to be an exciting time for those experts involved in critical care medicine and the field of functional genomics. Our team is hard at work planning an exceptional conference that blends key sessions, with non-competing exhibit hours.

Please feel free to contact me at any time to discuss the exhibit program. I can be reached at 781-837-2826 or via email at carrie@strategicresults.com.

I look forward to your participation in the 2003 Exhibit.

Best regards,

Carrie Dunne Strategic Results

Exhibit Area Schedule

Friday, November 14, 2003 3pm – 6pm Monday, November 17, 2003 7am – 8am **Set up**

Monday, November 17, 2003 8am – 5pm Exhibit Area open

Monday, November 17, 2003 5pm – 6pm Dismantle

These hours are subject to change. A final schedule will be included in your Exhibitor Services Manual.



About the Second Annual Symposium

The Functional Genomics of Critical Illness and Injury conference will focus attention on both the integrative demands of critical care medicine and the need for close communication with experts in functional genomic technologies.

NIH sponsored its first Symposium on Functional Genomics of Critical Illness and Injury at the Clinical Center in April 2002. This gathering was sponsored jointly by the Clinical Center, NIGMS, NIAMS, NHLBI, NHGRI, and NIAID with the help of the NIH Foundation and support from four international medical societies. Health care providers, physiologists, molecular biologists, genomicists, and biostatisticians gathered for three days to discuss the impact of genomics and proteomics on the science and practice of critical care medicine.

Four hundred participants representing more than ten countries heard presentations spanning a range from genome to population. Thirty leaders in their respective fields spoke on topics such as the clinical epidemiology of critical illness and injury, biocomplexity, investigational therapies, genome-wide expression profiles in trauma and infection, functional aspects of genetic variability in the intensive care unit, genomic studies of host-pathogen interactions, applications for defense against bioterrorism, and the future of computational genomics.

The second symposium will once again bring together multidisciplinary critical care specialists (e.g., intensivists from internal medicine, surgery, pediatrics, and anesthesiology), microbiologists, molecular biologists, experts in high-throughput technologies, and computational scientists to discuss the application of functional genomic approaches to critical illness and injury. This symposium will focus on knowledge emerging from relevant functional genomic databases and provide a forum for the presentation of primary data from patients and models of critical illness. The section on proteomics will reflect new developments in this field, especially in novel protein signatures and biomarkers of pathologic states. Pharmacogenomics as it applies to critically ill and injured patients is another major area included in this year's event.



Exhibit Package		Exhibit Fee	
	Listing in the on-site Conference Program Exhibitor Directory	□ \$500 per exhibit space.	
	Complimentary registration for two participants. This provides access to all sessions, meals, and refreshments mentioned in the conference agenda.		
	6' exhibit table		
	Post-conference attendee list		



Application and Contract for Exhibit Space

Functional Genomics of Critical Illness and Injury

November 17, 2003 Natcher Conference Center National Institutes of Health Bethesda, Maryland 781-837-2826, voice 410-377-6429, fax

The Contract constitutes the		Strategic Results and bitor" and obliges Exhibitors per the
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Exhibitor Participants			
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Last Name:	First Name:		



Terms and Conditions

Exposition character. Exhibitor understands that the events set forth in the Schedule of Events are produced by Strategic Results and agrees to comply with the entire terms and conditions of this Contract. Exhibitor further agrees that this Contract is binding upon all parties, their respective heirs, personal representatives, successors and assigns and can be amended only in writing by parties hereto.

Subleasing and sharing of exhibit space. Exhibitor will not assign or sublet any portion of the space, nor permit individuals other than employees, agents or representatives of exhibitor to use the facilities provided. The Exhibitor will not display products or literature that are not regularly sold or distributed by it; however, with the prior approval of Strategic Results, such may be used to illustrate the application of its product.

Liability. Exhibitor agrees that Strategic Results, the hosting organization and their respective employees and agents are not liable for any theft, damage, or loss to or of the Exhibitor's property or for any injury that may occur to the Exhibitor, its agents or employees. Exhibitor shall have property damage insurance for the full replacement value of all its property and general liability insurance of no less than One Million Dollars. Strategic Results and the hosting organization shall be named as additional loss payees in such policy. Exhibitor agrees to indemnify and hold Strategic Results and the hosting organization and their respective employees and agents harmless from any and all claims, demands, judgments, settlement costs, attorney's fees or other expenses either directly or indirectly from or in connection with Exhibitor's participation in such event.

Event promotions. Pre-show advertising and promotions are at the sole discretion of Strategic Results and the hosting organization.

Sale of products. Exhibitor will not sell any product or service during the exhibitor hours.

Endorsements. Strategic Results and the hosting organization do not approve, endorse, or recommend the use of any specific commercial products or service. Exhibitor will not represent, advertise, communicate, or imply either verbally or in writing, that its products or services are approved, endorsed, or recommended by Strategic Results or the hosting organization.

Set-up, show, and breakdown. Unless otherwise specified, Exhibitor agrees to check in and set up his/her display 30 minutes prior to the beginning of the event and completely remove



his/her display from the building within 60 minutes following the completion of the event. Failure to check in by the start of the event may result in loss of space with the Exhibitor still being liable for full payment.

Fire department regulations. Exhibitors will comply with all fire and safety regulations enforced in the location of the event.

Souvenirs, premiums, samples, and prizes. Distribution of souvenirs, premiums, and samples of products is permitted provided there is no interference with other exhibits. Consent to give away items, including contest prizes, will be granted by and is at the sole discretion of Strategic Results and the hosting organization. Exhibitor acknowledges that some event locations may prohibit giveaways of all kinds.

Exhibit space assignment. Event reservations are taken on a first- come first- served basis according to receipt of completed contract. The assignment and location of exhibit space are solely within the discretion of Strategic Results.

Exhibitor cancellation. If Exhibitor wishes to cancel any show space for which he/she has contracted herein, the Exhibitor must do so in writing. In order to receive a full refund, notification must be received by Strategic Results no later than 15 days prior to the exhibit date. Written notice of cancellation received 14 days or less from the exhibit date obligates the Exhibitor to pay Strategic Results 100% of the contractual amount. If the Exhibitor fails to attend an expo for which it has contracted, the Exhibitor will pay Strategic Results 100% of the contractual amount. When a contract is executed with less than 15 days prior to the exhibit date, the Exhibitor waives its right to cancel and will be liable for full payment of the price for such exhibit.

Space requirements and restriction. One display space will include a minimum 6-foot by 2-foot table, tablecloth, and no electrical power. The Exhibitor is to display equipment and products that will conform to the limitations of the display space as stated above. All exhibits must be displayed within the contracted space and all Exhibitor activities must be conducted in such a way as not to infringe on the rights of other Exhibitors or offend visitors to the event. Strategic Results and the hosting organization reserve the right to reject, in whole or in part, and at any time, an exhibit which, in their sole opinions, is objectionable to Exhibitors or others. No liabilities or damages whatsoever against Strategic Results and the hosting organization or any of their employees, agents, representatives, or members shall be incurred because of such rejection.



Payment terms. Strategic Results will invoice Exhibitor fees upon receipt of this contract. Payment of invoices is due upon receipt of invoice. Invoices not paid within 45 days will lose all applicable discounts associated with the contracted shows and Exhibitor will pay all fees associated with collection effort including, but not limited to, attorney fees of 25% of the amount owed and interest charges at the highest rate allowed by law. Strategic Results reserves the right to deny exhibit space to all Exhibitors that have overdue account balances with Strategic Results.

Governing law and jurisdiction. This contract shall be governed by and subject to the laws of the State of Maryland and all matters, whether sounding in contract or in tort relating to the validity, construction, interpretation, and enforcement of this Contract, shall be determined in the circuit Court of Baltimore County, Maryland, which Court shall have exclusive jurisdiction and venue.

Damage to property. Exhibitor will not paint, tape, nail, screw, staple, drill, or tack anything to the walls, columns, floor, or ceiling of the building or adjoining displays. Exhibitor shall be solely responsible for all damage resulting from such actions.

Event cancellation. Strategic Results and the hosting organization, in their sole discretion, reserve the right to cancel any event at any time without any liability for the fulfillment of this contract and all fees paid by Exhibitor shall, in the sole discretion of Strategic Results, be either credited to future events or refunded. If the exposition or any part thereof is cancelled for any reason beyond the control of Strategic Results such as, but not limited to, damage or destruction to building, war, riots, strikes, termination by hosting organization, acts of government, or acts of God, Strategic Results is not obligated to refund any fees.